Reviewer's report

Title: A new method for determination of varicella-zoster virus immunoglobulin G avidity in serum and cerebrospinal fluid

Version: 1 Date: 11 June 2004

Reviewer: Ilkka Seppala

Reviewer's report:

General
The method is interesting. However, the merits of the method are not readable with the necessary accuracy.
The paper tries to make points of two improvements to preexisting antibody avidity measurement methods. Firstly, the authors make a highly interesting claim that urea hydrogen peroxide is a more resolving dissociating agent for weak antigen-antibody interactions than plain urea. The second claim is that their new calculation method gives more accurate final data output than previous mathematical treatments of raw data in avidity measurement.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
For the first claim there is data only in Figure 1. This data is presented as final affinity values. No primary data are presented. Therefore, there remains the possibility that the wider scatter of values with the plain urea washing method as compared to a single incubation with urea hydrogen peroxide, could be due to unoptimal setup in the plain urea experiment. One critical variable is the quality of urea solutions since urea is not stable. The quality should be controlled by electrical conductance measurement for both urea and urea hydrogen peroxide solutions. The role of hydrogen peroxide should be revealed by dissolving plain urea to 4 M strength in 13.6 % hydrogen peroxide solution (=the approximate result of dissolving 4 M urea-hydrogen peroxide). If the quality of urea is satisfactory, that solution should be equivalent to the 4 M urea-hydrogen peroxide solution. For comparison, the authors should present data from an experiment where there is just one incubation with plain 4 M urea in the same manner as urea peroxide was used.

For the second claim there is more data presented. The reader of the paper still misses a graphic presentation of the principle in the calculation. How much different is the present calculation as compared to the log-log line fitting used as the comparative method for "Avidity 1,2" in reference 15? Would the same primary data give equally exact final results in both of these straight line fitting methods? The worse CV% values for method "Avidity 1,2" in Table 2 seem to stem to a considerable extent from aberrant avidity values for the least diluted samples (uppermost line in Table). The educated guesses used for starting values for factors a through d in "Avidity 1,2" calculation may perhaps be not well placed for the strongest sample dilution? Could this be commented?
On how many measurements are Table 1 CV% values based?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Introduction: Is there previous knowledge on the effect of replacing water with hydrogen peroxide in protein-protein interactions and protein hydrogen bonding?
Page 7, line9: "the relationship ....is linear ": upon dilution of samples?
Page 12, second chapter: There is no real solubility problem in 5 M urea. This cannot be used as a point in favor of urea hydrogen peroxide.
Discretionary Revisions (which the author can choose to ignore)
The Title of the paper is not informative of the points of basic interest in the paper. If the role of hydrogen peroxide in dissociation of protein-protein interactions could be confirmed, it would merit to be seen in the Title.
Page 7, bottom: In an ideal case the value for factor c should be near zero. Can factor c be used for quality control of the data?

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
None